

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Ann M. Lees et al. Art Unit :
Serial No. : Unassigned Examiner :
Filed : Herewith
Title : NOVEL LOW DENSITY LIPOPROTEIN BINDING PROTEINS AND THEIR
USE IN DIAGNOSING AND TREATING ATHEROSCLEROSIS

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows.

In the Specification:

Replace the paragraph beginning at page 1, line 5, with the following rewritten paragraph:

--This application is a divisional of U.S. Patent Application No. 09/616,289, filed July 14, 2000, which is a continuation-in-part of U.S. Patent Application No. 09/517,849, filed March 2, 2000, which is a continuation-in part of U.S. Patent Application No. 08/979,608, filed November 26, 1997, which claimed priority from U.S. Provisional Application No. 60/031,930, filed November 27, 1996, and U.S. Provisional Application No. 60/048,547, filed June 3, 1997. These applications are incorporated herein by reference in their entirety.--

Replace the paragraph beginning at page 6, line 7, with the following rewritten paragraph:

--Fig. 3 depicts the amino acid sequence of amino acids 319 to 550 of rabbit LBP-2 (SEQ ID NO: 3).--

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October 17, 2001
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Henry Jenkins
Signature

Henry Jenkins
Typed or Printed Name of Person Signing Certificate

Replace the paragraph beginning at page 6, line 9, with the following rewritten paragraph:

--Fig. 4 depicts the amino acid sequence of amino acids 299 to 550 of rabbit LBP-2 (SEQ ID No: 4).--

Replace the paragraph beginning at page 6, line 28, with the following rewritten paragraph:

--Fig. 10 depicts the cDNA sequence encoding rabbit LBP-1 (SEQ ID NO: 10) and the corresponding amino acid sequence (SEQ ID NO:1). Differences in amino acids between rabbit and human LBP-1 are depicted in bold type.--

Replace the paragraph beginning at page 6, line 31, with the following rewritten paragraph:

--Fig. 11 depicts a cDNA sequence encoding a portion of rabbit LBP-2 (SEQ ID NO: 11) and the corresponding amino acid sequence (SEQ ID NO:2). Differences in amino acids between rabbit and human LBP-2 are depicted in bold type. Where the sequences depicted in Fig. 2A and Fig. 11 differ, Fig. 2A represents the rabbit LBP-2 sequence.--

Replace the paragraph beginning at page 7, line 4, with the following rewritten paragraph:

--Fig. 12 depicts a cDNA sequence of nucleotides 256 to 1617 (SEQ ID NO: 12) of SEQ ID NO: 11 of rabbit LBP-2 and the corresponding amino acid sequence (SEQ ID NO:3).--

Replace the paragraph beginning at page 7, line 6, with the following rewritten paragraph:

--Fig. 13 depicts a cDNA sequence of nucleotides 196 to 1617 (SEQ ID NO: 13) of SEQ ID NO: 11 of rabbit LBP-2 and the corresponding amino acid sequence (SEQ ID NO:4).--

Replace the paragraph beginning at page 7, line 8, with the following rewritten

paragraph:

--Fig. 14 depicts the cDNA sequence encoding rabbit LBP-3 (SEQ ID NO: 14) and the corresponding amino acid sequence (SEQ ID NO:5). Differences in amino acids between rabbit and human LBP-3 are depicted in bold type.--

Replace the paragraph beginning at page 7, line 11, with the following rewritten paragraph:

--Fig. 15 depicts the cDNA sequence encoding human LBP-1 (SEQ ID NO: 15) and the corresponding amino acid sequence (SEQ ID NO:6). Differences in amino acids between rabbit and human LBP-1 are depicted in bold type.--

Replace the paragraph beginning at page 7, line 14, with the following rewritten paragraph:

--Fig. 16 depicts a cDNA sequence encoding a portion of human LBP-2 (SEQ ID NO: 16) and the corresponding amino acid sequence (SEQ ID NO:7). Differences in amino acids between rabbit and human LBP-2 are depicted in bold type.--

Replace the paragraph beginning at page 7, line 17, with the following rewritten paragraph:

--Fig. 17 depicts a cDNA sequence encoding a portion of human LBP-3 (SEQ ID NO: 17) and the corresponding amino acid sequence (SEQ ID NO:8). Differences in amino acids between rabbit and human LBP-3 are depicted in bold type. Where the sequences depicted in Fig. 8A and Fig. 17 differ, Fig. 8A represents the human LBP-3 sequence.--

Replace the paragraph beginning at page 7, line 21, with the following rewritten paragraph:

--Fig. 18 depicts the cDNA sequence encoding BHF-1 (SEQ ID NO: 18) and corresponding amino acid sequence (SEQ IDNO:9).--

Replace the paragraph beginning at page 7, line 22, with the following rewritten

paragraph:

--Fig. 19 corresponds to the amino acid sequence of rabbit LBP-1 (top sequence; SEQ ID NO:1) in alignment with the amino acid sequence of human LBP-1 (bottom sequence; SEQ ID NO:6).--

Replace the paragraph beginning at page 7, line 24, with the following rewritten paragraph:

--Fig. 20 corresponds to the amino acid sequence of a portion of the amino acid sequence of rabbit LBP-2 (top sequence; amino acid residues 331-550 of SEQ ID NO:47) in alignment with a portion of the amino acid sequence of human LBP-2 (bottom sequence; SEQ ID NO:7).--

Replace the paragraph beginning at page 7, line 27, with the following rewritten paragraph:

--Fig. 21 corresponds to the amino acid sequence of rabbit LBP-3 (top sequence; SEQ ID NO:5) in alignment with the amino acid sequence of a portion of human LBP-3 (bottom sequence; SEQ ID NO:44).--

Replace the paragraph beginning at page 7, line 30, with the following rewritten paragraph:

--Fig. 22 depicts the genomic sequence of human LBP-1 (SEQ ID NO:49) and corresponding amino acid sequence (SEQ ID NO:6).--

Replace the paragraph beginning at page 7, line 31, with the following rewritten paragraph:

--Fig. 23 depicts the genomic sequence of human LBP-2 (SEQ ID NO:50) and corresponding amino acid sequence (SEQ ID NO:43).--

Replace the paragraph beginning at page 8, line 1, with the following rewritten paragraph:

--Fig. 24 depicts the genomic sequence of human LBP-3 (SEQ ID NO:51) and

corresponding amino acid sequence (SEQ ID NO:44).--

Replace the paragraph beginning at page 8, line 11, with the following rewritten paragraph:

--This invention provides for an isolated polynucleotide comprising a polynucleotide encoding the polypeptide having the amino acid sequence of rabbit LBP-1 as set forth in Fig. 1 (SEQ ID NO: 1); rabbit LBP-2 as set forth in Fig. 2A (SEQ ID NO: 47); a portion of rabbit LBP-2 as set forth in Fig. 2B (SEQ ID NO: 2); 319 to 550 of rabbit LBP-2 as set forth in Fig. 3 (SEQ ID NO: 3); 299 to 550 of rabbit LBP-2 as set forth in Fig. 4 (SEQ ID NO: 4); rabbit LBP-3 as set forth in Fig. 5 (SEQ ID NO: 5); human LBP-1 as set forth in Fig. 6 (SEQ ID NO: 6); human LBP-2 as set forth in Fig. 7A (SEQ ID NO: 43); 322 to 538 of human LBP-2 as set forth in Fig. 7B (SEQ ID NO: 7); human LBP-3 as set forth in Fig. 8A (SEQ ID NO: 44); 17-546 of human LBP-3 as set forth in Fig. 8B (SEQ ID NO: 8); 14 to 33 of human (SEQ ID NO:6) or rabbit (SEQ ID NO:1) LBP-1, called BHF-1, as set forth in Fig. 9 (SEQ ID NO: 9); a polynucleotide capable of hybridizing to and which is at least about 80% identical, more preferably at least about 90% identical, more preferably yet at least about 95% identical, and most preferably at least about 98% identical to any of the above polynucleotides, and wherein the encoded polypeptide is capable of binding to LDL; or a biologically active fragment of any of the above polynucleotides wherein the encoded polypeptide is capable of binding to LDL.--

Replace the paragraph beginning at page 11, line 26, with the following rewritten paragraph:

--This invention also includes an isolated polypeptide comprising a polypeptide having amino acid residues 329-343 (SEQ ID NO: 19), 329-354 (SEQ ID NO: 20), 344-354 (SEQ ID NO: 21) or 529-538 (SEQ ID NO: 22) as set forth in Fig. 7A (SEQ ID NO: 47); amino acid residues 14-43 (SEQ ID NO: 23) or 38-43 (SEQ ID NO: 24) as set forth in Fig. 1 (SEQ ID NO: 1) and Fig. 6 (SEQ ID NO: 6); amino acid residues 338-353 (SEQ ID NO: 25), 338-365 (SEQ ID NO: 26), 354-365 (SEQ ID NO: 27) or 444-453 (SEQ ID NO: 28) as set forth in Fig. 2A (SEQ ID NO: 47); amino acid residues 96-110 (SEQ ID NO: 29) as set forth in Fig. 5 (SEQ ID NO: 5); and amino acid residues 69-75 (SEQ ID NO: 41) as set forth in Fig. 8A (SEQ ID NO:44); or a

polypeptide which is at least about 80% identical, more preferably at least about 90% identical, more preferably yet at least about 95% identical, and most preferably at least about 98% identical to the above polypeptides, and wherein said polypeptide is capable of binding to LDL; or a biologically active fragment of any of the above polypeptides wherein the fragment is capable of binding to LDL.--

Replace the paragraph beginning at page 34, line 3, with the following rewritten paragraph:

--Thus, a diagnostic embodiment of the invention is the adaptation of, e.g., a peptide complementary to one of the LBPs, by radiolabeling it and using it as an injectable imaging agent for detection of occult atherosclerosis. The peptide is selected from those known to bind to LBPs, e.g., RRRRRRRR (SEQ ID NO:52) or KKLKLXX (SEQ ID NO:53), or any other polycationic peptide which binds to the highly electronegative domains of the LBPs. For extracorporeal detection with a gamma scintillation (Anger) camera, technetium-binding ligands, e.g., CGC, GGCGC, or GGCGCF, can be incorporated into the peptides at the N-terminus or C-terminus for ^{99m}Tc labeling. For external imaging by magnetic resonance imaging (MRI), e.g., the gadolinium-binding chelator, diethylene triamine penta-acetic acid (DTPA), is covalently bound to the N- or C-terminus of the peptides. In yet other embodiments, the LBP-binding peptides are covalently bound, e.g., to magnetic ion oxide particles by standard methods known to those skilled in the art, e.g., conjugating the peptides with activated polystyrene resin beads containing magnetic ion oxide.--

In the Claims:

Add new claims 38-104.

--38. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence that is at least about 80% identical to the sequence of SEQ ID NO:2, wherein the polypeptide binds to LDL.

39. The nucleic acid of claim 38, wherein the amino acid sequence is at least about 90% identical to the sequence of SEQ ID NO:2.

40. The nucleic acid of claim 38, wherein the amino acid sequence is at least about 95% identical to the sequence of SEQ ID NO:2.

41. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the sequence of SEQ ID NO:2.

42. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence that is at least about 80% identical to the sequence of SEQ ID NO:7, wherein the polypeptide binds to LDL.

43. The nucleic acid of claim 42, wherein the amino acid sequence is at least about 90% identical to the sequence of SEQ ID NO:7.

44. The nucleic acid of claim 42, wherein the amino acid sequence is at least about 95% identical to the sequence of SEQ ID NO:7.

45. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the sequence of SEQ ID NO:7.

46. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence that is at least about 80% identical to the sequence of SEQ ID NO:43, wherein the polypeptide binds to LDL.

47. The nucleic acid of claim 46, wherein the amino acid sequence is at least about 90% identical to the sequence of SEQ ID NO:43.

48. The nucleic acid of claim 46, wherein the amino acid sequence is at least about 95% identical to the sequence of SEQ ID NO:43.

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49. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the sequence of SEQ ID NO:43.

50. The nucleic acid of claim 49, wherein the polypeptide consists of the sequence of SEQ ID NO:43.

51. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence that is at least about 80% identical to the sequence of SEQ ID NO:47, wherein the polypeptide binds to LDL.

52. The nucleic acid of claim 51, wherein the amino acid sequence is at least about 90% identical to the sequence of SEQ ID NO:47.

53. The nucleic acid of claim 51, wherein the amino acid sequence is at least about 95% identical to the sequence of SEQ ID NO:47.

54. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the sequence of SEQ ID NO:47.

55. The nucleic acid of claim 54, wherein the polypeptide consists of the sequence of SEQ ID NO:47.

56. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and is at least about 80% identical to a portion of the sequence of SEQ ID NO:2 or SEQ ID NO:7 that binds to LDL.

57. The nucleic acid of claim 56, wherein the amino acid sequence is at least about 90% identical to a portion of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:7.

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58. The nucleic acid of claim 56, wherein the amino acid sequence is at least about 95% identical to a portion of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:7.

59. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and is at least about 80% identical to a portion of the sequence of SEQ ID NO:43 or SEQ ID NO:47 that binds to LDL.

60. The nucleic acid of claim 59, wherein the amino acid sequence is at least about 90% identical to a portion of the amino acid sequence of SEQ ID NO:43 or SEQ ID NO:47.

61. The nucleic acid of claim 59, wherein the amino acid sequence is at least about 95% identical to a portion of the amino acid sequence of SEQ ID NO:43 or SEQ ID NO:47.

62. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence identical to a fragment of at least ten amino acid residues of SEQ ID NO:2.

63. The nucleic acid of claim 62, wherein the polypeptide binds to LDL.

64. The nucleic acid of claim 62, wherein the amino acid sequence is identical to a fragment of at least about 20 amino acid residues of SEQ ID NO:2.

65. The nucleic acid of claim 62, wherein the amino acid sequence is identical to a fragment of at least about 30 amino acid residues of SEQ ID NO:2.

66. The nucleic acid of claim 62, wherein the amino acid sequence comprises SEQ ID NO:3 SEQ ID NO:4, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, or SEQ ID NO:28.

67. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence identical to a fragment of at least ten amino acid residues of SEQ ID NO:7.

68. The nucleic acid of claim 67, wherein the polypeptide binds to LDL.

69. The nucleic acid of claim 67, wherein the amino acid sequence is identical to a fragment of at least about 20 amino acid residues of SEQ ID NO:7.

70. The nucleic acid of claim 67, wherein the amino acid sequence is identical to a fragment of at least about 30 amino acid residues of SEQ ID NO:7.

71. The nucleic acid of claim 67, wherein the amino acid sequence comprises SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

72. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence identical to a fragment of at least ten amino acid residues of SEQ ID NO:43.

73. The nucleic acid of claim 72, wherein the polypeptide binds to LDL.

74. The nucleic acid of claim 72, wherein the amino acid sequence is identical to a fragment of at least about 20 amino acid residues of SEQ ID NO:43.

75. The nucleic acid of claim 72, wherein the amino acid sequence is identical to a fragment of at least about 30 amino acid residues of SEQ ID NO:43.

76. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence identical to a fragment of at least ten amino acid residues of SEQ ID NO:47.

77. The nucleic acid of claim 76, wherein the polypeptide binds to LDL.

78. The nucleic acid of claim 76, wherein the amino acid sequence is identical to a fragment of at least about 20 amino acid residues of SEQ ID NO:47.

79. The nucleic acid of claim 76, wherein the amino acid sequence is identical to a fragment of at least about 30 amino acid residues of SEQ ID NO:47.

80. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and differs by one or more conservative amino acid substitutions from the sequence of SEQ ID NO:2 or SEQ ID NO:7.

81. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and differs by one or more conservative amino acid substitutions from the sequence of SEQ ID NO:43 or SEQ ID NO:47.

82. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least ten amino acid residues of SEQ ID NO:2 or SEQ ID NO:7.

83. The nucleic acid of claim 82, wherein the amino acid sequence differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least about 20 amino acid residues of SEQ ID NO:2 or SEQ ID NO:7.

84. The nucleic acid of claim 82, wherein the amino acid sequence differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least about 30 amino acid residues of SEQ ID NO:2 or SEQ ID NO:7.

85. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence, wherein the amino acid sequence binds to LDL and differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least ten amino acid residues of SEQ ID NO:43 or SEQ ID NO:47.

86. The nucleic acid of claim 85, wherein the amino acid sequence differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least about 20 amino acid residues of SEQ ID NO:43 or SEQ ID NO:47.

87. The nucleic acid of claim 85, wherein the amino acid sequence differs by one or more conservative amino acid substitutions from the sequence of a fragment of at least about 30 amino acid residues of SEQ ID NO:43 or SEQ ID NO:47.

88. An isolated nucleic acid comprising a nucleotide sequence that specifically hybridizes to the sequence of SEQ ID NO:11 or SEQ ID NO:16.

89. The nucleic acid of claim 88, wherein the nucleotide sequence encodes a polypeptide that binds to LDL.

90. The nucleic acid of claim 88, wherein the nucleotide sequence is at least about 80% identical to the sequence of SEQ ID NO:11 or SEQ ID NO:16.

91. The nucleic acid of claim 88, wherein the nucleotide sequence is at least about 95% identical to the sequence of SEQ ID NO:11 or SEQ ID NO:16.

93. An isolated nucleic acid comprising a nucleotide sequence that specifically hybridizes to the sequence of SEQ ID NO:45 or SEQ ID NO:48.

94. The nucleic acid of claim 93, wherein the nucleotide sequence encodes a polypeptide that binds to LDL.

95. The nucleic acid of claim 93, wherein the nucleotide sequence is at least about 80% identical to the sequence of SEQ ID NO:45 or SEQ ID NO:48.

96. The nucleic acid of claim 93, wherein the nucleotide sequence is at least about 95% identical to the sequence of SEQ ID NO:45 or SEQ ID NO:48.

97. The nucleic acid of claim 93, wherein the nucleotide sequence comprises the sequence of SEQ ID NO:45 or SEQ ID NO:48.

98. An isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, or SEQ ID NO:33.

99. A recombinant vector comprising the nucleic acid of claim 38.

100. A recombinant vector comprising the nucleic acid of claim 42.

101. A cell comprising the recombinant vector of claim 99.

102. A cell comprising the recombinant vector of claim 100.

103. A method of producing a polypeptide, the method comprising culturing the cell of claim 101 under conditions that permit expression of the polypeptide.

104. A method of producing a polypeptide, the method comprising culturing the cell of claim 102 under conditions that permit expression of the polypeptide.

Cancel claims 1-37 without prejudice.

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REMARKS

Claims 38-104 are pending in the application, claims 1-37 having been cancelled without prejudice and claims 38-104 having been added by the above amendment. Support for new claims 38-104 can be found, e.g., in original claims 1-14 and in the specification at: page 2, lines 19-30; page 8, line 11, to page 11, line 13; page 17, line 7, to page 18, line 15; and page 27, line 1, to page 28, line 3. These amendments add no new matter.

The present application is a divisional of U.S. Patent Application No. 09/616,289, filed July 14, 2000. The claims of this divisional application are directed to LBP-2 nucleic acids, recombinant vectors, host cells, and methods of producing LBP-2 polypeptides. The claims of the parent application (Serial No. 09/616,289) are directed to LBP-2 polypeptides.

CONCLUSIONS

Attached is a marked-up version of the changes being made by the current amendment. Applicants ask that all claims be examined.

Enclosed is a check for the basic filing fee and claims fees. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 10797-004002.

Respectfully submitted,

Date: October 12, 2001

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Version with Markings to Show Changes Made

In the Specification:

The paragraph beginning at page 1, line 5, has been amended as follows:

This application is a divisional of U.S. Patent Application No. 09/616,289, filed July 14, 2000, which is a continuation-in-part of U.S. Patent Application No. [USPN] 09/517,849, filed March 2, 2000, which is [was] a continuation-in part of U.S. Patent Application No. [USPN] 08/979,608, filed November 26, 1997, which claimed priority from U.S. Provisional Application No. [USPN] 60/031,930, filed November 27, 1996, and U.S. Provisional Application No. [USPN] 60/048,547, filed June 3, 1997. These applications are incorporated herein by reference in their entirety.

The paragraph beginning at page 6, line 7, has been amended as follows:

Fig. 3 depicts the amino acid sequence of amino acids 319 to [350] 550 of rabbit LBP-2 (SEQ ID NO: 3).

The paragraph beginning at page 6, line 9, has been amended as follows:

Fig. 4 depicts the amino acid sequence of amino acids 299 to [350] 550 of rabbit LBP-2 (SEQ ID No: 4).

The paragraph beginning at page 6, line 28, has been amended as follows:

Fig. 10 depicts the cDNA sequence encoding rabbit LBP-1 (SEQ ID NO: 10) and the corresponding amino acid sequence (SEQ ID NO:1). Differences in amino acids between rabbit and human LBP-1 are depicted in bold type.

The paragraph beginning at page 6, line 31, has been amended as follows:

Fig. 11 depicts a cDNA sequence encoding a portion of rabbit LBP-2 (SEQ ID NO: 11) and the corresponding amino acid sequence: (SEQ ID NO:2). Differences in amino acids between rabbit and human LBP-2 are depicted in bold type. Where the sequences depicted in Fig. 2A and

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Fig. 11 differ, Fig. 2A represents the rabbit LBP-2 sequence.

The paragraph beginning at page 7, line 4, has been amended as follows:

Fig. 12 depicts a cDNA sequence of nucleotides 256 to 1617 (SEQ ID NO: 12) of SEQ ID NO: 11 of rabbit LBP-2 and the corresponding amino acid sequence (SEQ ID NO:3).

The paragraph beginning at page 7, line 6, has been amended as follows:

Fig. 13 depicts a cDNA sequence of nucleotides 196 to 1617 (SEQ ID NO: 13) of SEQ ID NO: 11 of rabbit LBP-2 and the corresponding amino acid sequence (SEQ ID NO:4).

The paragraph beginning at page 7, line 8, has been amended as follows:

Fig. 14 depicts the cDNA sequence encoding rabbit LBP-3 (SEQ ID NO: 14) and the corresponding amino acid sequence (SEQ ID NO:5). Differences in amino acids between rabbit and human LBP-3 are depicted in bold type.

The paragraph beginning at page 7, line 11, has been amended as follows:

Fig. 15 depicts the cDNA sequence encoding human LBP-1 (SEQ ID NO: 15) and the corresponding amino acid sequence (SEQ ID NO:6). Differences in amino acids between rabbit and human LBP-1 are depicted in bold type.

The paragraph beginning at page 7, line 14, has been amended as follows:

Fig. 16 depicts a cDNA sequence encoding a portion of human LBP-2 (SEQ ID NO: 16) and the corresponding amino acid sequence (SEQ ID NO:7). Differences in amino acids between rabbit and human LBP-2 are depicted in bold type.

The paragraph beginning at page 7, line 17, has been amended as follows:

Fig. 17 depicts a cDNA sequence encoding a portion of human LBP-3 (SEQ ID NO: 17) and the corresponding amino acid sequence (SEQ ID NO:8). Differences in amino acids between rabbit and human LBP-3 are depicted in bold type. Where the sequences depicted in Fig. 8A and Fig. 17 differ, Fig. 8A represents the human LBP-3 sequence.

The paragraph beginning at page 7, line 21, has been amended as follows:

Fig. 18 depicts the cDNA sequence encoding BHF-1 (SEQ ID NO: 18) and corresponding amino acid sequence (SEQ IDNO:9).

The paragraph beginning at page 7, line 22, has been amended as follows:

Fig. 19 corresponds to the amino acid sequence of rabbit LBP-1 (top sequence; SEQ ID NO:1) in alignment with the amino acid sequence of human LBP-1 (bottom sequence; SEQ ID NO:6).

The paragraph beginning at page 7, line 24, has been amended as follows:

Fig. 20 corresponds to the amino acid sequence of a portion of the amino acid sequence of rabbit LBP-2 (top sequence; amino acid residues 331-550 of SEQ ID NO:47) in alignment with a portion of the amino acid sequence of human LBP-2 (bottom sequence; SEQ ID NO:7).

The paragraph beginning at page 7, line 27, has been amended as follows:

Fig. 21 corresponds to the amino acid sequence of rabbit LBP-3 (top sequence; SEQ ID NO:5) in alignment with the amino acid sequence of a portion of human LBP-3 (bottom sequence; SEQ ID NO:44).

The paragraph beginning at page 7, line 30, has been amended as follows:

Fig. 22 depicts the genomic sequence of human LBP-1 (SEQ ID NO:49) and corresponding amino acid sequence (SEQ ID NO:6).

The paragraph beginning at page 7, line 31, has been amended as follows:

Fig. 23 depicts the genomic sequence of human LBP-2 (SEQ ID NO:50) and corresponding amino acid sequence (SEQ ID NO:43).

The paragraph beginning at page 8, line 1, has been amended as follows:

Fig. 24 depicts the genomic sequence of human LBP-3 (SEQ ID NO:51) and

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corresponding amino acid sequence (SEQ ID NO:44).

The paragraph beginning at page 8, line 11, has been amended as follows:

This invention provides for an isolated polynucleotide comprising a polynucleotide encoding the polypeptide having the amino acid sequence of rabbit LBP-1 as set forth in Fig. 1 (SEQ ID NO: 1); rabbit LBP-2 as set forth in Fig. 2A (SEQ ID NO: 47); a portion of rabbit LBP-2 as set forth in Fig. 2B (SEQ ID NO: 2); 319 to [350] 550 of rabbit LBP-2 as set forth in Fig. 3 (SEQ ID NO: 3); 299 to [350] 550 of rabbit LBP-2 as set forth in Fig. 4 (SEQ ID NO: 4); rabbit LBP-3 as set forth in Fig. 5 (SEQ ID NO: 5); human LBP-1 as set forth in Fig. 6 (SEQ ID NO: 6); human LBP-2 as set forth in Fig. 7A (SEQ ID NO: 43); 322 to 538 of human LBP-2 as set forth in Fig. 7B (SEQ ID NO: 7); human LBP-3 as set forth in Fig. 8A (SEQ ID NO: 44); 17-546 of human LBP-3 as set forth in Fig. 8B (SEQ ID NO: 8); 14 to 33 of human (SEQ ID NO:6) or rabbit (SEQ ID NO:1) LBP-1, called BHF-1, as set forth in Fig. 9 (SEQ ID NO: 9); a polynucleotide capable of hybridizing to and which is at least about 80% identical, more preferably at least about 90% identical, more preferably yet at least about 95% identical, and most preferably at least about 98% identical to any of the above polynucleotides, and wherein the encoded polypeptide is capable of binding to LDL; or a biologically active fragment of any of the above polynucleotides wherein the encoded polypeptide is capable of binding to LDL.

The paragraph beginning at page 11, line 26, has been amended as follows:

This invention also includes an isolated polypeptide comprising a polypeptide having amino acid residues 329-343 (SEQ ID NO: 19), 329-354 (SEQ ID NO: 20), 344-354 (SEQ ID NO: 21) or 529-538 (SEQ ID NO: 22) as set forth in Fig. 7A (SEQ ID NO: 47); amino acid residues 14-43 (SEQ ID NO: 23) or 38-43 (SEQ ID NO: 24) as set forth in Fig. 1 (SEQ ID NO: 1) and Fig. 6 (SEQ ID NO: 6); amino acid residues 338-353 (SEQ ID NO: 25), 338-365 (SEQ ID NO: 26), 354-365 (SEQ ID NO: 27) or 444-453 (SEQ ID NO: 28) as set forth in Fig. 2A (SEQ ID NO: 47); amino acid residues 96-110 (SEQ ID NO: 29) as set forth in Fig. 5 (SEQ ID NO: 5); and amino acid residues 69-75 (SEQ ID NO: 41) as set forth in Fig. 8A (SEQ ID NO: [8] 44); or a polypeptide which is at least about 80% identical, more preferably at least about 90% identical, more preferably yet at least about 95% identical, and most preferably at least about 98% identical

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to the above polypeptides, and wherein said polypeptide is capable of binding to LDL; or a biologically active fragment of any of the above polypeptides wherein the fragment is capable of binding to LDL.

The paragraph beginning at page 34, line 3, has been amended as follows:

Thus, a diagnostic embodiment of the invention is the adaptation of, e.g., a peptide complementary to one of the LBPs, by radiolabeling it and using it as an injectable imaging agent for detection of occult atherosclerosis. The peptide is selected from those known to bind to LBPs, e.g., RRRRRRRR (SEQ ID NO:52) or KKLKLXX (SEQ ID NO:53), or any other polycationic peptide which binds to the highly electronegative domains of the LBPs. For extracorporeal detection with a gamma scintillation (Anger) camera, technetium-binding ligands, e.g., CGC, GGCGC, or GGCGCF, can be incorporated into the peptides at the N-terminus or C-terminus for ^{99m}Tc labeling. For external imaging by magnetic resonance imaging (MRI), e.g., the gadolinium-binding chelator, diethylene triamine penta-acetic acid (DTPA), is covalently bound to the N- or C-terminus of the peptides. In yet other embodiments, the LBP-binding peptides are covalently bound, e.g., to magnetic ion oxide particles by standard methods known to those skilled in the art, e.g., conjugating the peptides with activated polystyrene resin beads containing magnetic ion oxide.

In the Claims:

Claims 1-37 have been cancelled without prejudice.